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LETTER TO THE EDITORS

Tuberculous enteritis: a surgical 'Janus' masquerading as intestinal obstruction

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Dear Sirs,

Tuberculosis (TB) still represents a major morbidity and mortality cause during the post-transplant (PT) period among transplant recipients. Lungs are commonly involved. In renal transplant (RT) recipients, extrapulmonary (occurring in 15%) and disseminated diseases (33–49%) are very frequent [1], while intestinal involvement is extremely rare, with a reported prevalence between 0.2% and 0.6% [2]. Atypical presentation is the rule in immunocompromised patients, while high clinical suspicion is required. In immunosuppressed patients, the ulcerative component of disease is predominant due to decreased inflammatory response, rather than bowel wall inflammation with obstruction, making gastrointestinal bleeding the most common presenting symptom [2]. Despite this fact, bowel obstruction along with perforation was the initial manifestation in our case.

A 46-year-old man underwent deceased-donor RT (01/08) for IgA-nephropathy end-stage renal disease (Donor-CMV+/Recipient-CMV+). Induction therapy (IT) included daclizumab. Panel-reactive antibodies were 0%. Because of delayed renal graft function, hemodialysis required during the early PT period. He was discharged on the 19th postoperative day with creatinine level of 1.9 mg/dl. Four months PT, creatinine levels remained stable, while 24-h urine protein levels reached 532 mg/dl. Renal graft biopsy revealed changes of acute T-cell mediated rejection (ACR) (i1t1). Treatment with a 3-day course of i.v. pulses of 500 mg methylprednisolone and appropriate tapering followed. There was no change in the immunosuppressive regimen (ISR) afterward. Six years following RT he presented with acute abdominal pain and fever, distended abdomen and diffuse abdominal tenderness. Abdominal CT scan showed thickening of the wall of the terminal ileum with obstruction and enlarged mesenteric lymph nodes (Fig. 1a). Exploratory laparotomy revealed large quantities of purulent fluid, due to distal ileal perforation. Two palpable masses, occluding the lumen partially were detected. Segmental ileal resection was performed. Pathological investigation suggested the diagnosis of TB ileitis. Tissue specimens obtained from the resected bowel segment revealed few visible bacilli on acid-fast-stain (AFB). Macroscopic study of the resected specimen revealed caseous necrotic material and multiple ileal mucosa ulcerations (Fig. 1b). Microscopic examination showed submucosal granulomas with gigantic cells and caseous necrosis (Fig. 1c and d). Thoracic CT scan revealed no other focuses. Gastric aspirate culture, AFB and PCR, as well as blood culture and PCR of the surgical wound drainage were negative for TB. Escherichia coli was detected in the peritoneal fluid and blood culture and i.v. Meropenem was initiated according to the sensitivity, parallel to the anti-TB treatment with isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (ETH). One week later patient remained febrile despite treatment and started deteriorating rapidly with intractable fevers, profound weakness, and hemodynamic instability. Abdominal CT scan revealed a walled-off subhepatic abscess. Exploratory laparotomy was performed, where a subcapsular–subhepatic infected hematoma, requiring partial liver resection of segment-VII, was removed. During surgery patient became hemodynamically unstable and after appropriate liver packing and initial resuscitation, he was admitted to the ICU. Unpacking of the liver was performed 48 h later. Pathological study of the resected liver specimen revealed granulomas around portal triads, characteristic for TB. After his admission to the ICU, patient started to develop abnormal liver function tests (LFT's), (AST 152 U/l and ALT 168 U/l) and high levels of total bilirubin up to 10 mg/dl. It was decided to discontinue RIF, INH, and PZA and planned to reintroduce alternate anti-TB agents sequentially, adding 1 agent per week with closely LFT's monitoring. His condition improved progressively while LFT's normalized within 2 weeks; he was discharged afebrile with a plan to be seen weekly.

Mycobacterium Tuberculosis (MT) is a well-known opportunistic agent following RT. Risk factors for PT–TB are diabetes mellitus, previous rejection episodes, rejection treatment with antilymphocyte globulin and bolus corticosteroids, IT with anti-CD25 agents and maintenance therapy

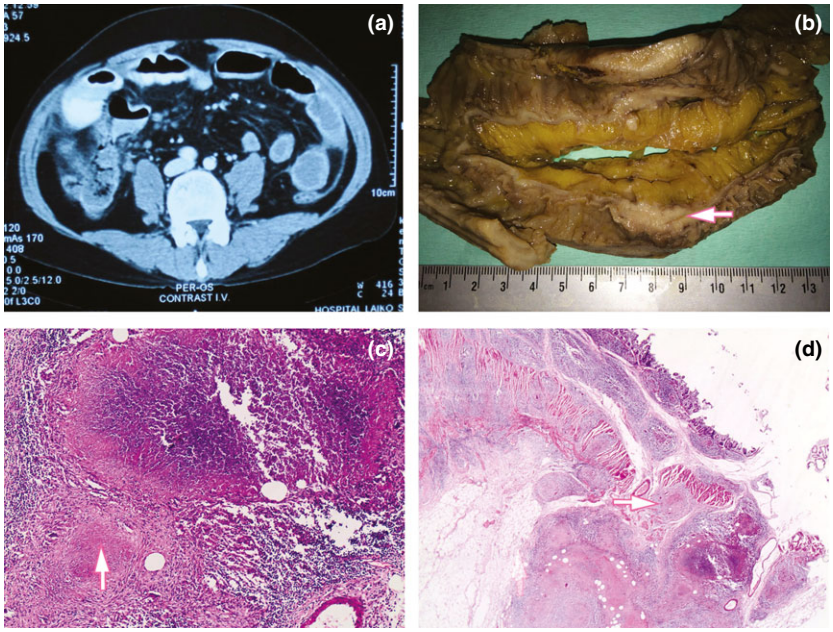

Figure 1 (a) Preoperative CT image showing dilated loops of small bowel. (b) Macroscopic appearance of caseous necrosis of the resected surgical specimen (arrow). (c) Caseating granuloma (arrow) characteristic of tuberculosis (H&E stain). (d) Caseating granuloma (arrow) and ulceration of the adjacent mucosa of the small bowel (H&E stain).

with corticosteroids [2]. In our case, patient was not diabetic, received daclizumab as IT and had a history of an ACR-episode, that was treated with bolus corticosteroids. Cylex immuknow assay levels were obtained at rejection time (541 ng/ml). No recent test results are available to correlate changes in T-cell activation with the relative risk of opportunistic agent infection. ISR during infection contained tacrolimus 3 mg/day, MMF 1440 mg/day, and methylprednisolone 4 mg/day. There was no recent travel history. His pretransplant tuberculin skin test and chest x-ray were negative. Family members were tested following diagnosis confirmation, while his father found to have a highly reactive tuberculin skin test, along with x-ray pulmonary infiltrates indicative of prior inactive TB.

Gastrointestinal manifestation is infrequent, but potentially lethal. It appears frequently during the early PT period [1]. Commonly, it is presented with atypical and vague symptoms such as abdominal pain, fever, weight loss. Intestinal obstruction and perforation are extremely rare, while ileocecal region is the commonest site [3]. Radiographic studies may assist in making diagnosis of gastrointestinal tuberculosis (GITB), but the definitive diagnosis involves the isolation of the bacilli [4]. In immunosuppressed patients, TB is frequent, rapidly disseminates and appropriate therapy should be instituted as early as possible when there is a high degree of suspicion even in the absence of MT isolation [2]. PT–TB poses high mortality which is mostly related to co-existing infections and side effects of anti-TB treatment, mainly hepatic failure [4], while GITB-associated mortality varies between 20% and 30% and must always be taken into account when treating RT patients [1].

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Conflicts of interest

The authors have declared no conflicts of interest.

References

1. Azevedo P, Freitas C, Silva H, *et al.* A case series of gastrointestinal tuberculosis in renal transplant recipients. *Case Rep Nephrol* 2013; **2013**: 213273.
2. Jarrett O, Grim SA, Benedetti E, Clark NM. Gastrointestinal tuberculosis in renal transplant recipients: case report and review of the literature. *Transpl Infect Dis* 2011; **13**: 52.
3. Ulloa JG, Parekh J, Hope C, Roll GR. Case report of intestinal tuberculosis 6 years after simultaneous pancreas and kidney transplant. *Transplant Proc* 2014; **46**: 2450.
4. Chan HW, Cheung CY, Chan YH, *et al.* Intestinal tuberculosis as a cause of gastrointestinal bleeding in a renal transplant recipient. *Transpl Int* 2010; **23**: 657.